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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
2000 GALLOPING HILL ROAD
KENILWORTH, NJ 07033-0530

EXAMINER	
WANG, SHENGJUN	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/057,534
Filing Date: January 25, 2002
Appellant(s): DAVIS ET AL.

Ann Marie Cannoni
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed August 2, 2005 appealing from the Office action mailed March 24, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is essentially correct except that Claims 12-27 and 34 have been withdrawn from further consideration as drawn to non-elected invention and/or species. Claim 12-27 and 34 were inadvertently listed as rejected claim in prior office action. Claim 34 is actually directed to a method claim, and does not read on the elected composition. Further, claims 12-27 have been withdrawn from further consideration as drawn to non-elected species. The elected third active ingredient is simvastatin, claims 8-11 read on the elected species. See restriction requirements mailed July 16, 2003. The claims have been examined are those read on elected invention and species.

This appeal involves claims 1-3, 5, 6, 8-11, 28, 31-33, 35, 36, 70-72, 74-77, 79 and 80.

Claims 29, 30, 34, 39, 41, 44, 46, 49, 51, 54, 59, 64, 66, 69, 73, 78, 81 are withdrawn from further consideration as being drawn to a nonelected invention, claims 4, 12-27, 37, 38, 40, 42-43, 45, 47-48, 50, 52-43, 55-58, 60-63, 65, 67-68 are withdrawn from further consideration as being drawn to a nonelected species.

Claim 7 has been canceled.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

A substantially correct copy of appealed claims 1-3, 5, 6, 8-12, 28, 31-33, 35-36, 70-72,74-77,79 and 80 appears on pages 21-31 of the Appendix to the appellant's brief. The minor errors are as follows: claims 12-27 and 34 are not appealed claims.

(8) Evidence Relied Upon

The following is a listing of the evidence (e.g., patents, publications, Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal.

US Patent 5,846,966	Rosenblum et al.	December 8, 2005
US Patent 5,300,288	Albright	April 5, 1994
US Patent 5,661,145	Davis	August 26, 1997
US Patent 4,837,255	Dechow	June 6, 1989

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

1. Claims 1-3, 5, 6, 8-12, 28, 31-33, 35, 36,70-72, 74-77 and 79-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (US 5,846,966, IDS) in view of Albright (US 5,300,288), Dechow (US 4,837,255), and Davis (US 5,661,145, IDS).

Rosenblum teaches the instant cholesterol absorption inhibitors and its application for lowering serum cholesterol. Rosenblum further teaches that the cholesterol absorption inhibitors may be employ in combination with other cholesterol lowering agents, such as simvastatin. See, particularly, the abstract, and the claims (claim 5 is directed to the elected sterol absorption inhibitor, ezetimibe). Rosenblum et al. teach that daily dosage of the compounds is about 5mg to 1000 mg, given in a single dose or 2-4 divided doses. When used in combination with other drug the dose is about 1mg to 1000 mg a dose given 1 or 2 times a day. The exact dose would depend on various conditions. See, particularly, col. 21, lines 17-63.

2. Rosenblum et al. does not teach expressly a combination of a hydroxy-substituted azetidinone compounds, e.g., ezetimibe, and a bile acid sequestrant, e.g., cholestyramine, or further with a cholesterol biosynthesis inhibitor, e.g., simvastatin.

3. However, as shown in Albright, cholestyramine is an old and well-known cholesterol-lowering agent. See, column 2, lines 3-7. Dechow particularly, teaches a method of lowering cholesterol by administering to a patient a composition comprising cholestyramine. See, particularly, the claims. Davis teaches that simvastatin is a known cholesterol biosynthesis inhibitor, and is particularly useful with lactam cholesterol absorption inhibitor. See, particularly, column 2, lines 51-63.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to make cholesterol lowering composition comprising the hydroxy-substituted azetidinone compound, ezetimibe, and the well-known cholesterol lowering agent, cholestyramine.

A person of ordinary skill in the art would have been motivated to make cholesterol lowering composition comprising the hydroxy-substituted azetidinone compound, ezetimibe, and the well-known cholesterol lowering agent, cholestyramine. It is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus, the claimed invention which is a combination of two known cholesterol lowering agent sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069. The further employment of simvastatin in the combination is obvious because the hydroxy-substituted azetidinone compounds are known to be useful with cholesterol biosynthesis inhibitor. Further, the optimization of a result effective parameter, e.g., effective amount of a therapeutical agent, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215.

As to the specific amount of ezetimibe, note the amount (10 mg) is within the range disclosed by Rosenblum et al. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Further, Optimization Within Prior Art Conditions or Through Routine Experimentation Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

(10) Response to Arguments

In response to appellant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the teaching, suggestion and motivation are found in the cited references and in the knowledge generally available to one of ordinary skill in the art. Particularly, the cited references teach that all the active ingredients herein are known to be useful for lowering cholesterol. The references further teach that is known to combine different cholesterol lowering agents for treating hypercholesterolemia. It is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art.

4. Appellants argue that In re Kerkoven was misused in the rejections because the ingredients in the claimed combination function through different biochemical mechanisms. The arguments are unpersuasive. Even though the detailed biological functions of those ingredients may be different, the ultimate results are the same, i.e., lowering the level of cholesterol. Therefore, ingredients herein have been known to one of ordinary skill in ten art as therapeutical

agents used for the very same purpose, i.e., lowering the level of cholesterol. Further, the cited references have suggested the use of different cholesterol lowering agents together. For examples, Rosenblum et al. teaches the combination of sterol absorption inhibitor with HMG CoA reductase inhibitors. See, column 6, line 37-50, claims 5.

Appellants' arguments fail to reach the instant rejections core issue; that concomitantly employing compounds, old and well known for the same use is obvious to the skilled artisan. This is particularly true in the art for treating hypercholesterolemia, where combination of different types of cholesterol lowering agents are commonly used.

As discussed above, the amount (10 mg) of sterol absorption inhibitor is within the range disclosed by Rosenblum et al. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Further, Optimization Within Prior Art Conditions or Through Routine Experimentation Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Shengjun Wang
SHENGJUN WANG
PRIMARY EXAMINER

Conferees:

THURMAN K. PAGE, M.A., J.D
SUPERVISORY PATENT EXAMINER

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER